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Sir:

Transmitted herewith for filing is a provisional patent application under 37 CFR 1.53(c) of:

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Title: BIOLOGICAL DESIGN AUTOMATION SYSTEM

Enclosed are:
- ☒ 13 pages of the specification (including description and claims).
- ☒ 5 sheet(s) of drawing(s).
- ☒ 1 Exhibits
- ☒ Abstract
- ☐ A verified statement to establish small entity status under 37 CFR 1.9 and 37 CFR 1.27.
- ☐ The invention was made by or under a contract with the following agency of the United States Government: _____ under Government contract number: _____.
- ☐ Please record the enclosed assignment to: _____

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Respectfully submitted,

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PROVISIONAL

PATENT APPLICATION

BIOLOGICAL DESIGN AUTOMATION SYSTEM

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BIOLOGICAL DESIGN AUTOMATION SYSTEM

CROSS-REFERENCES TO RELATED APPLICATIONS

This application is related to, and incorporates herein by reference the entire disclosures of, the following previously filed provisional patent applications: U.S. provisional patent application no. 60/141,503 filed June 28, 1999, U.S. provisional patent application no. 60/147,199 filed August 3, 1999, and U.S. provisional patent application no. 60/186,856 filed March 3, 2000.

BACKGROUND OF THE INVENTION

The present invention relates to a biological design automation system. The system may employ microfabricated structures and microfabricated systems for regulating fluid-flow. Various approaches to designing micro-fluidic pumps and valves are known. Such micro-fluidic devices can be used for fluid analysis for example, of biological samples.

The analysis of fluids such as clinical or environmental fluids generally involves a series of processing steps, which may include chemical, optical, electrical, mechanical, thermal, or acoustical processing of the fluid samples. Whether incorporated into a bench-top instrument, a disposable cartridge, or a combination of the two, such processing typically involves complex fluidic assemblies and processing algorithms.

The fluid analysis systems for processing fluid samples typically employ a series of chambers each configured for subjecting the fluid sample to a specific processing step. As the fluid sample flows through the system sequentially from chamber to chamber, the fluid sample undergoes the processing steps according to a specific protocol. Because different protocols require different configurations, the design and manufacturing of such systems can be time-consuming and costly.

SUMMARY OF THE INVENTION

A design automation system provides the relevant functional methods of design, analysis, and implementation of single or multi-layer soft lithography networks, or microfluidic channels, of elastomeric circuits or chips. Utilization of such a design automation system can lead to implementing simple to highly complex elastomeric

networks for use in general fluidic transfer control systems, biological diagnostics systems, etc., quickly and easily. Henceforth the design automation system will be referred to as the Biological Design Automation ("BDA") system.

The elastomeric circuit employs microfluidic devices such as on/off valves, switching valves, and pumps made out of various layers of elastomer bonded together. In a preferred aspect, the present invention uses a multilayer soft lithography process to build integrated (i.e., monolithic) microfabricated elastomeric structures. Advantages of fabricating the elastomeric structures by binding together layers of soft elastomeric materials include the fact that the resulting devices are reduced by more than two orders of magnitude in size as compared to silicon-based devices. Further advantages of rapid prototyping, ease of fabrication, and biocompatability are also achieved.

In accordance with an aspect of the present invention, a fluidic circuit design method comprises selecting and connecting components according to a design. The components include fluidic components. The method further comprises functionally simulating selected components of the design, arranging the components into a physical layout according to the design, and physically simulating the components in the physical layout.

In some embodiments, the fluidic components comprise microfluidic components. The microfluidic components are selected from the group consisting of channels, pumps, valves, chambers, and layer interconnects. The components are selected from normalized, custom, pre-defined, and user-defined components. The components are connected according to preset design rules. The components are assigned physical scaling and physical properties. The selected components are active fluidic components.

In specific embodiments, the selected components of the design are functionally simulated by applying control signals to the selected active fluidic components to show functional connectivity of the design. To functionally simulate selected components of the design, active fluidic components are defined as Boolean expressions with operands based on control ports of the active fluidic components which control connections to input ports and output ports of the active fluidic components. Actuation of the active fluidic components is simulated using control signals generated by a Boolean based language with timing constraints. The design may be modified based on results of the functional simulation.

In some embodiments, arranging the components into a physical layout comprises placing and routing the components according to the design. The components are placed interactively or automatically using a layout tool based on preset design rule constraints. The components are placed based on mechanical properties thereof. The components are routed interactively or automatically using a autorouting tool based on preset rules.

In specific embodiments, physically simulating the components in the physical layout comprises at least one of analyzing dynamic volumetric flow rates in the components, analyzing volumetric capacitances of the components, and analyzing volumetric capacitances of interconnecting and routing channels in the physical layout. Physically simulating the components of the physical layout may include simulating actuation of dynamic fluid flow in the components using control signals generated by a Boolean based language. The physical layout may be modified based on results of the physical simulation. The method may include writing the physical layout to a layout file to be used for manufacturing.

In accordance with another aspect of the invention, a fluidic circuit design system comprises a design capture module including a schematic entry tool for selecting and connecting components according to a design. The components including fluidic components. The system further comprises a functional analysis module for functionally simulating selected components of the design, a physical implementation module for arranging the components into a physical layout according to the design, and a physical analysis module for physically simulating the components in the physical layout.

In some embodiments, the modules comprise instructions stored in a computer-readable medium. The computer-readable medium is operatively coupled to a computer network to permit access to the instructions via the computer network. The computer-readable medium may be operatively coupled to the Internet to permit access to the instructions via the Internet.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a block diagram of the biological design automation system according to an embodiment of the present invention;

Figure 2 is a block diagram illustrating design capture in the design automation system of Figure 1;

Figure 3 is a block diagram illustrating functional analysis in the design automation system of Figure 1;

Figure 4 is a block diagram illustrating physical implementation in the design automation system of Figure 1;

Figure 5 is a block diagram illustrating physical analysis in the design automation system of Figure 1; and

Figure 6 is a block diagram illustrating device implementation in the design automation system of Figure 1.

DESCRIPTION OF THE SPECIFIC EMBODIMENTS

The BDA system 10 shown in Figure 1 represents the system at a block level and comprises four primary phases (phases 1, 2, 4, and 6) and two secondary phases (phases 3 and 5). Design conception 100 is the first step (phase 1) where the desired functionality of the microfluidic channels and networks is defined. Once the functionality has been defined the second primary step 200 (phase 2) is to capture the resulting network schematically using basic predefined components, macro components from a library, or user-defined components. The third primary step 400 (phase 4) is the physical implementation of the design and involves the physical placement and connections of the networks from a two and three dimensional perspective. The fourth, and final, primary step 600 (phase 6) is the actual creation of the circuit. Two secondary phases are shown as well and are used at different points of the BDA system 10. These secondary phases are the functional and physical analysis of the described designs. Functional analysis 300 (phase 3) aides the designer in verifying the desired function of the design. Physical analysis 500 (phase 5) allows the designer to verify and analyze the dynamic performance of the design. While functional and physical analysis are not as important for simple low component count design, they become extremely crucial for moderately complex to highly complex designs by minimizing the need to empirically test and redesign until the desired network is achieved.

I. CONCEPTION

The elastomeric circuit or chip design begins with the conception of the desired functionality to achieve using devices that include microfluidic devices including microfluidic channels, pumps, networks, and the like. In one preferred embodiment, the

microfluidic devices are those described in the document attached herewith as Exhibit 1. Of course, the present invention is not limited to those microfluidic devices.

II. DESIGN CAPTURE

Once the design has been conceptually defined, it can be then be captured using a schematic entry tool 202 that is used to select the components and connect between the input/output ports of components (Figure 2). The schematic entry tool 202 enables the quick creation of designs through the use of the following:

- Predefined Basic Library Components 206
  - Valves (normalized, custom, pre-defined)
  - Pumps (normalized, custom, pre-defined)
  - Lenses (normalized, custom, pre-defined)
  - Mixing Chambers (normalized, custom, pre-defined)
  - Input Chambers (normalized, custom, pre-defined)
  - Output/Waste Chambers (normalized, custom, pre-defined)
  - Layer interconnects (vias) (normalized, custom, pre-defined)
  - Etc.
- Macro Library 210
  - Cell sorter macro (normalized, custom, pre-defined)
  - DNA Finger printing macro (normalized, custom, pre-defined)
  - Etc.
- Property assignments for components 214
  - Physical Scaling of normalized components
  - Physical Properties of normalized components
    - Thermal
    - Conductivity
    - Viscosity
    - Magnetic
  - Layer Assignment
  - Functional (digital/analog) description – if necessary or desired
  - Hierarchical net and component user defined naming scheme
  - Design rule specification for layout
- Schematic Entry Tool Features of Tool 202
  - Search and replace

- Drag and drop
- Snap to grid, etc.

As shown in Figure 2, the design capture step 200 produces a design database 220 that represents the interconnected components and to which physical layers the components are assigned.

III. FUNCTIONAL ANALYSIS

After completion of the schematic design entry, a good design practice leading to reduce the number of design iterations would be to functionally simulate the design. Functional simulation of microfluidic circuits involves application of control signals to the active components of the design and shows the functional/static connectivity of the design without regard to the dynamic behavior of the fluid within the device. Examples of active fluidic components include valves and pumps which act on the fluid. A fixed channel is an example of a passive fluidic component. Functional libraries 302 for the component models are provided for each component or defined for a user-defined component as part of the properties of the component, as shown in Figure 1. Figure 3 shows the block diagram of the functional analysis 300 of the BDA system 10.

A. Functional Libraries

A functional design model 310 is developed by functional extraction of the schematic design database 220. The functional libraries of the basic components and macro components are defined as Boolean expressions with operands based on the control port(s) 316 of the active component which control connections to the input ports 312 and the output ports 314. Valid Boolean operators are as follows: * = AND, + = OR, ^ = XOR, ! = NOT.

For example, a simple valve component with a single input port and a single output port and a control port can be defined as follows:

Input = I, Output = O, Control = C
Functional Model Valve
Port I: *input*
Port O: *output*
Port C: *control*
$O = I * C$

B. Functional Simulation

Logical fluidic flow simulation 306 of the logic control 304 of the testing apparatus that will actuate the active components (Figure 1) will be created using the Diagnostic Device Control Language or Diagnostic Chip Control Language (DCCL), as shown in Figure 3. The DCCL is a simple Boolean based language with timing constraints that can generate control signals to simulate actuation of the device's active components and read and log data from detection ports 318 of the functional design model 310. Additional physical characteristics of the control and input signals can be included for the physical simulation but ignored in the functional simulation. Consequently, the same DCCL program can be used in the actual testing when the device is ultimately fabricated and put into use by the designer.

The output static analysis result 330 of the functional analysis is displayed from the BDA system 10 as a series of square waves that indicate valve position, path connectivity, detection, control signal generation, etc.

IV. PHYSICAL IMPLEMENTATION

Once the schematic design has been completed and functionally tested, the physical implementation of the schematic into a layout takes place, as shown in Figure 4. While the schematic representation of the design was arranged to be readable in the design database 220, the physical layout 410 is arranged to be functional, so there is typically little correlation between the schematic and the layout. The design database 220 represents the interconnected components and to which physical layers the components are assigned. Each layer of the microfluidic circuit are placed and routed such that each of the components is connected as designed.

A. Physical Layout

There are two primary aspects to the physical layout 410 of the microfluidic device. The first is component placement and the second is the routing of the interconnections between the placed components.

Components can be either interactively placed or automatically placed in the BDA system's layout tool. The layout tool has the following features:

- Ability to group components by connectivity by layer and/or by cross layer (3D grouping)

- Place components based on design rule constraints (DRC) in the DRC database 424 from set mechanical properties per layer provided in the mechanical properties library 422, and perform design rule checking 420
- Allow for grid and gridless placement of components
- Highlighting DRC errors
- Layer to layer shrinkage compensation for placements
- Read and write the DWG and DXF file formats
- Etc.

Routing the components can be either interactively or automatically done in the BDA system's routing tool. The routing tools has the following features:

- Definition of routing cross-sectional profiles
- Autorouting 430 for similarly pitched components – grid or gridless
- Definition/Optimization of routing corners: right angle, radius, etc.
- Relocation of routing to other layers
- Layer to layer shrinkage compensation for routing
- Read and write the DWG and DXF file formats
- Etc.

B. Manufacturing Support

Once the design has been completely placed and routed the BDA system 10 will write out the desired chip layout files to manufacture the microfluidic device. The DWG/DXF files written from the place and route portion can be converted to the following manufacturing formats for use in device implementation 600 (see Figure 1):

- Gerber
- HPGL
- Postscript
- Etc.

V. PHYSICAL ANALYSIS

Once the design has been completed, placed, and routed, a simulation indicating the dynamic performance can be performed. As shown in Figure 1, dynamic simulation models 510 of the components are based on the physical attributes as well as the chosen material properties for the layer in which the component is placed, as provided in the mechanical properties library 512. Fluid characteristics are also taken into account

as well as the control signal's actual actuation pressures. The following highlights some of the possible physical analysis in the BDA system 10:

- Dynamic volumetric flow rates
- Volumetric capacitances of components
- Volumetric capacitances of interconnect/routing channels
- Parasitic layout extraction 520
- Parasitic components
- Etc.

Dynamic fluidic flow simulation 530 may employ a DCCL file 532 as shown in Figure 5, which may be the same as the DCCL 320 used in the functional analysis 300. The dynamic model 510 includes basic components and macro components that are defined as Boolean expressions with operands based on the control port(s) 516 of the active component which control connections to the input ports 512 and the output ports 514. The DCCL is a simple Boolean based language with timing constraints that can generate control signals to simulate actuation of the device's active components and read and log data from detection ports 318 of the dynamic model 510. The physical analysis 500 produces output dynamic analysis result 540.

VI. DEVICE IMPLEMENTATION

As shown in Figure 1, the chip layout file 602 produced from physical implementation 400 can be used for prototype manufacturing 604.

The BDA system 10 can be implemented and executed in a variety of ways. For instance, it can be implemented as a computer-aided design (CAD) program for design, analysis, and implementation of the elastomeric circuits or networks. The CAD program can be provided separately to individual users or distributed over networks such as the Internet so that it can be centrally maintained and controlled.

WHAT IS CLAIMED IS:

1. A fluidic circuit design method comprising:

selecting and connecting components according to a design, the components including fluidic components;

functionally simulating selected components of the design;

arranging the components into a physical layout according to the design; and

physically simulating the components in the physical layout.

2. The method of claim 1 wherein the fluidic components comprise microfluidic components.

3. The method of claim 2 wherein the microfluidic components are selected from the group consisting of channels, pumps, valves, chambers, and layer interconnects.

4. The method of claim 1 wherein the components are selected from normalized, custom, pre-defined, and user-defined components.

5. The method of claim 1 wherein the components are connected according to preset design rules.

6. The method of claim 1 wherein the components are assigned physical scaling.

7. The method of claim 1 wherein the components are assigned physical properties.

8. The method of claim 1 wherein the selected components are active fluidic components.

9. The method of claim 8 wherein the selected components of the design are functionally simulated by applying control signals to the selected active fluidic components to show functional connectivity of the design.

10. The method of claim 1 wherein functionally simulating selected components of the design comprises defining active fluidic components as Boolean

expressions with operands based on control ports of the active fluidic components which control connections to input ports and output ports of the active fluidic components.

11. The method of claim 10 wherein functionally simulating selected components of the design comprises simulating actuation of the active fluidic components using control signals generated by a Boolean based language with timing constraints.

12. The method of claim 1 wherein arranging the components into a physical layout comprises placing the components according to the design.

13. The method of claim 12 wherein the components are placed automatically using a layout tool based on preset design rule constraints.

14. The method of claim 12 wherein the components are placed interactively.

15. The method of claim 12 wherein the components are placed based on mechanical properties thereof.

16. The method of claim 1 wherein arranging the components into a physical layout comprises routing the components according to the design.

17. The method of claim 16 wherein the components are routed automatically using a autorouting tool based on preset rules.

18. The method of claim 16 wherein the components are routed interactively.

19. The method of claim 1 wherein physically simulating the components in the physical layout comprises at least one of analyzing dynamic volumetric flow rates in the components, analyzing volumetric capacitances of the components, and analyzing volumetric capacitances of interconnecting and routing channels in the physical layout.

20. The method of claim 1 wherein physically simulating the components of the physical layout comprises simulating actuation of dynamic fluid flow in the components using control signals generated by a Boolean based language.

21. The method of claim 1 further comprising modifying the design based on results of the functional simulation.

22. The method of claim 1 further comprising modifying the physical layout based on results of the physical simulation.

23. The method of claim 1 further comprising writing the physical layout to a layout file to be used for manufacturing.

24. A fluidic circuit design system comprising:

a design capture module including a schematic entry tool for selecting and connecting components according to a design, the components including fluidic components;

a functional analysis module for functionally simulating selected components of the design;

a physical implementation module for arranging the components into a physical layout according to the design; and

a physical analysis module for physically simulating the components in the physical layout.

25. The system of claim 24 wherein the modules comprise instructions stored in a computer-readable medium.

26. The system of claim 25 wherein the computer-readable medium is operatively coupled to a computer network to permit access to the instructions via the computer network.

27. The system of claim 26 wherein the computer-readable medium is operatively coupled to the Internet to permit access to the instructions via the Internet.

BIOLOGICAL DESIGN AUTOMATION SYSTEM

ABSTRACT OF THE DISCLOSURE

A design automation system provides the relevant functional methods of design, analysis, and implementation of single or multi-layer soft lithography networks, or microfluidic channels, of elastomeric circuits or chips. Utilization of such a design automation system can lead to implementing simple to highly complex elastomeric networks for use in general fluidic transfer control systems, biological diagnostics systems, etc., quickly and easily. An embodiment of the invention is directed to a fluidic circuit design method that comprises selecting and connecting components according to a design. The components include fluidic components. The method further comprises functionally simulating selected components of the design, arranging the components into a physical layout according to the design, and physically simulating the components in the physical layout. The physical layout is then used for prototype manufacturing.

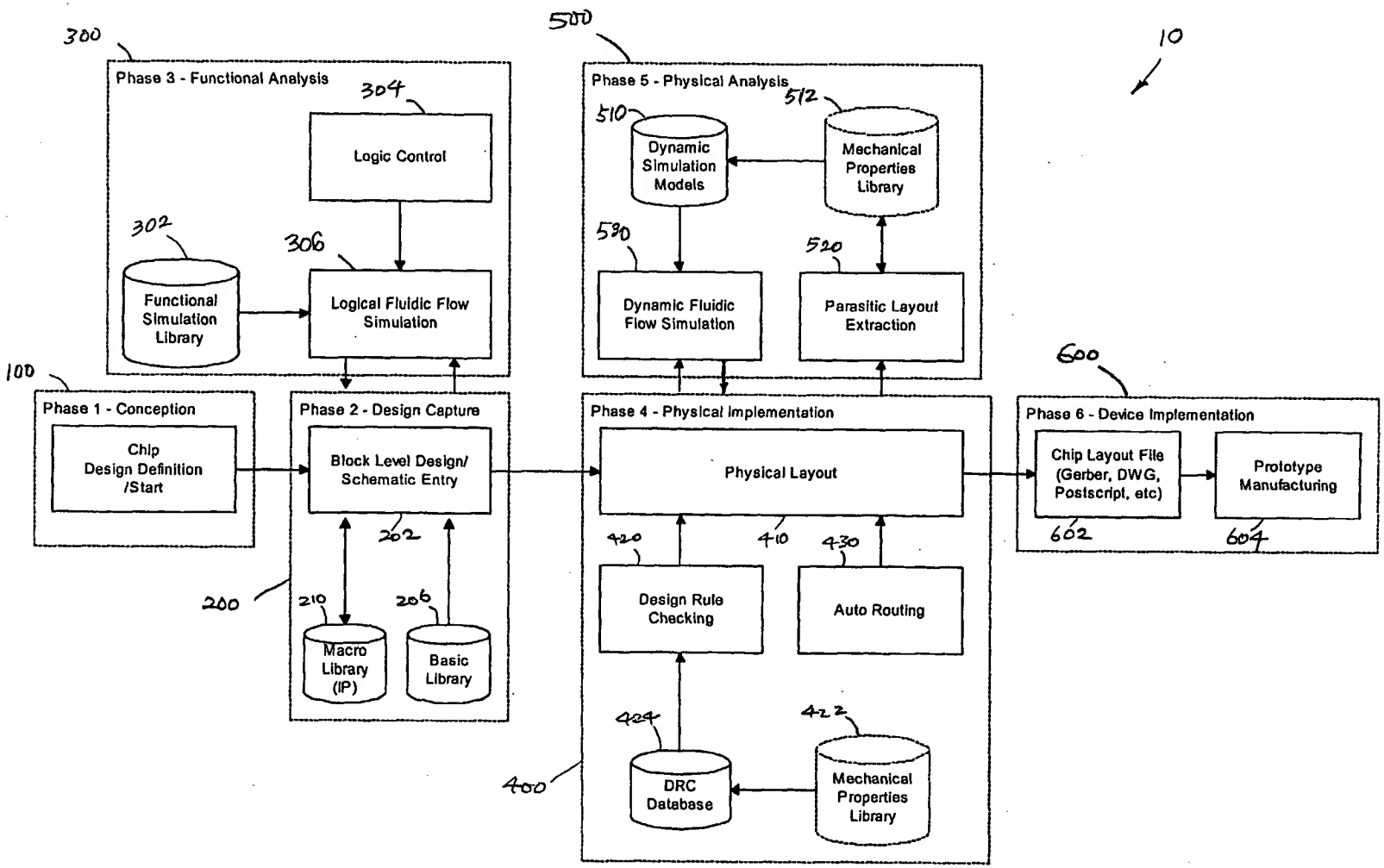

FIG. 1

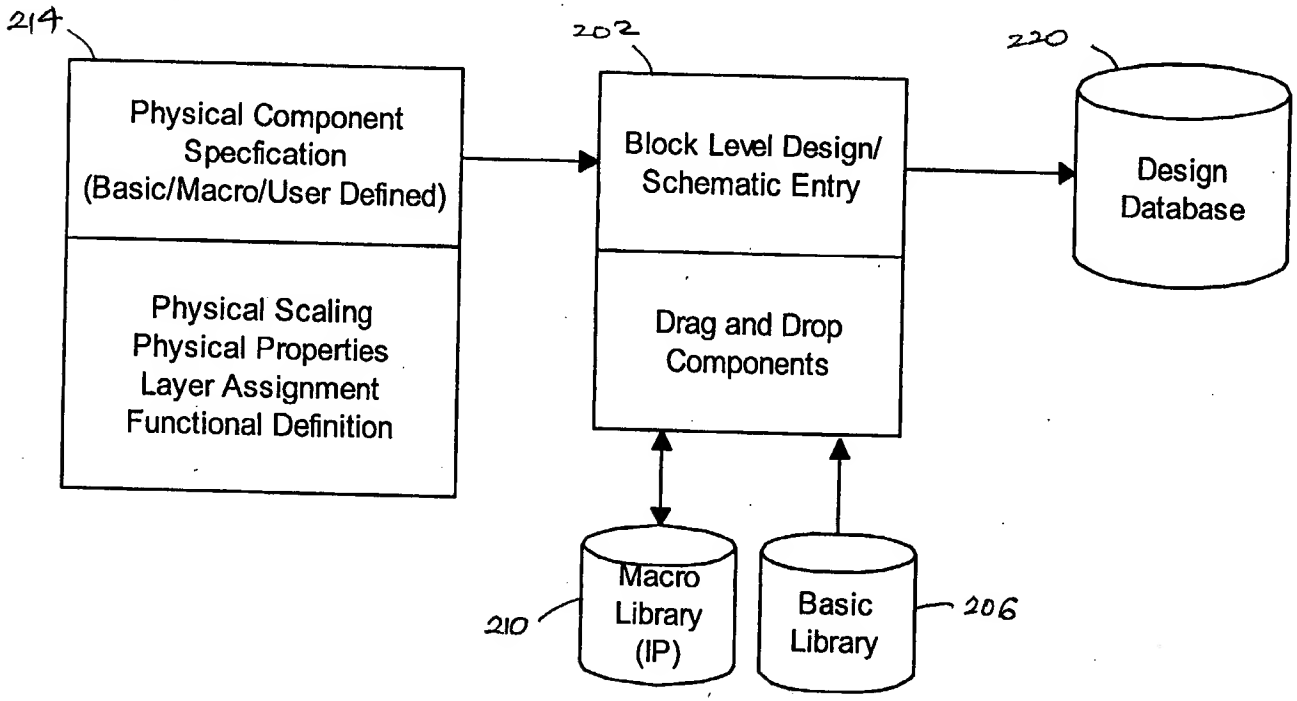

FIG. 2

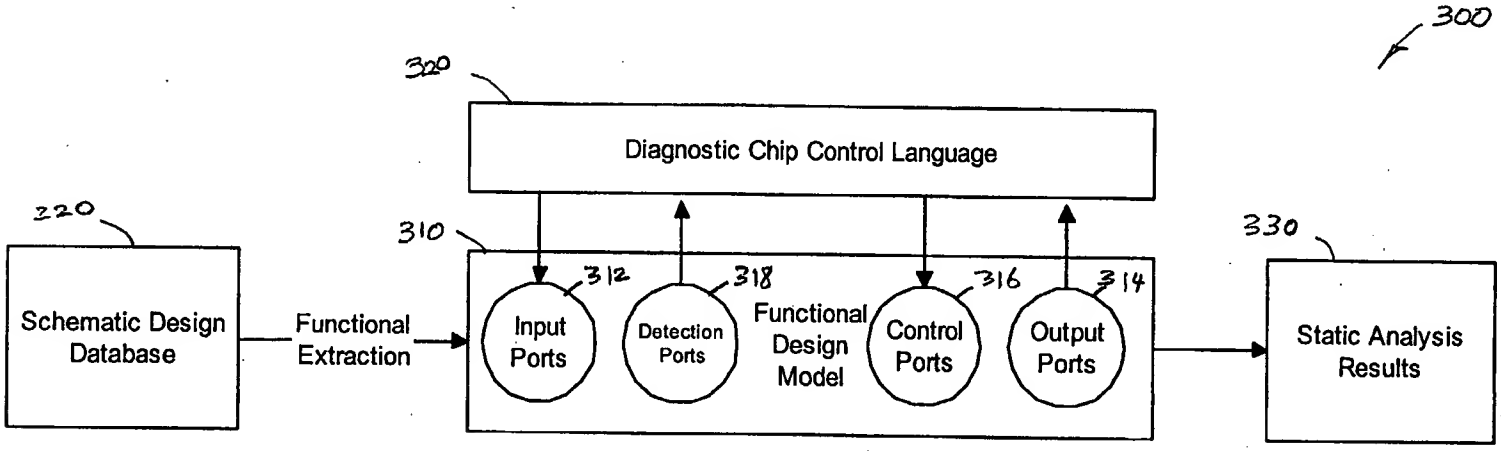

FIG. 3

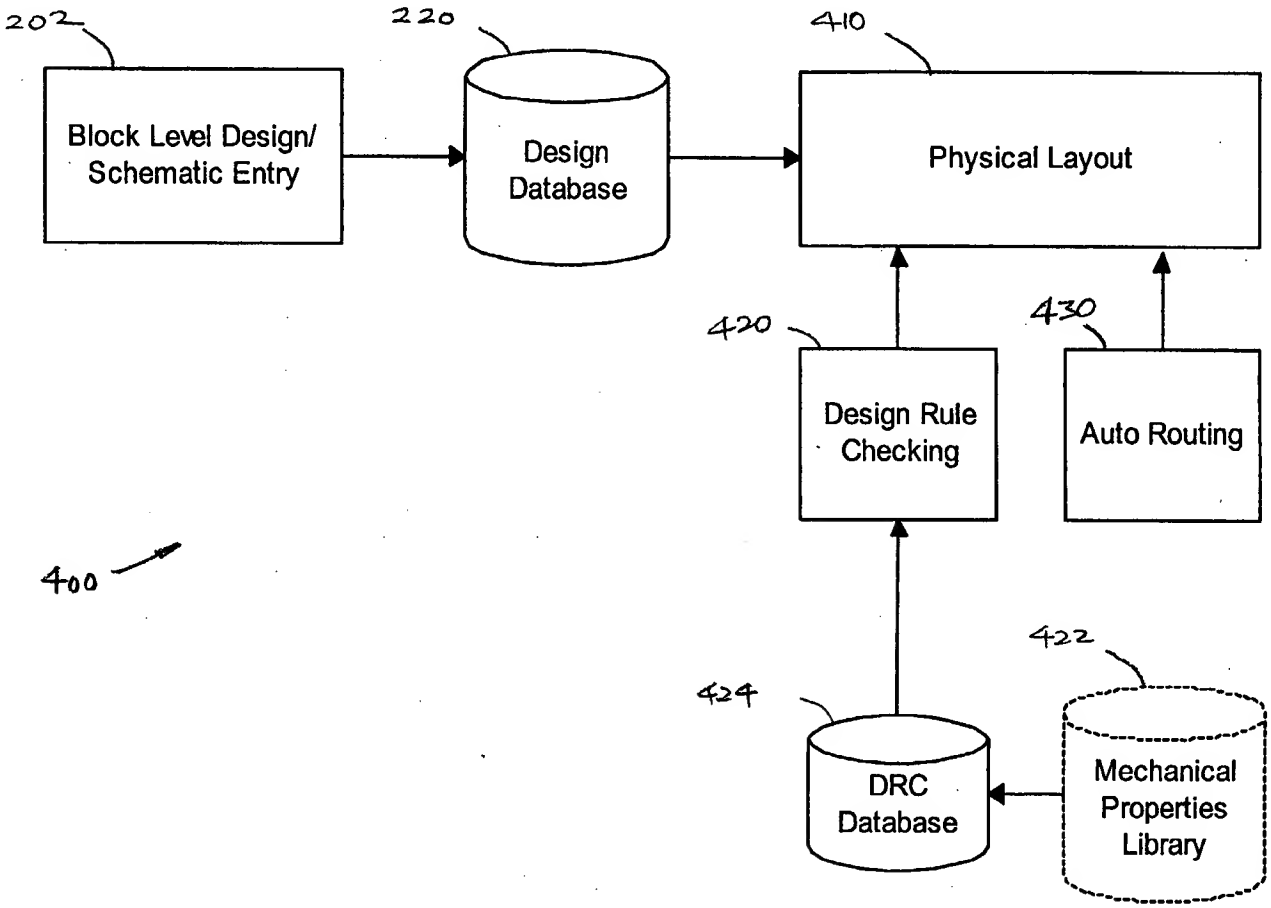
202
Block Level Design/
Schematic Entry
220
Design
Database
410
Physical Layout
420
Design Rule
Checking
430
Auto Routing
400
424
DRC
Database
422
Mechanical
Properties
Library

FIG. 4

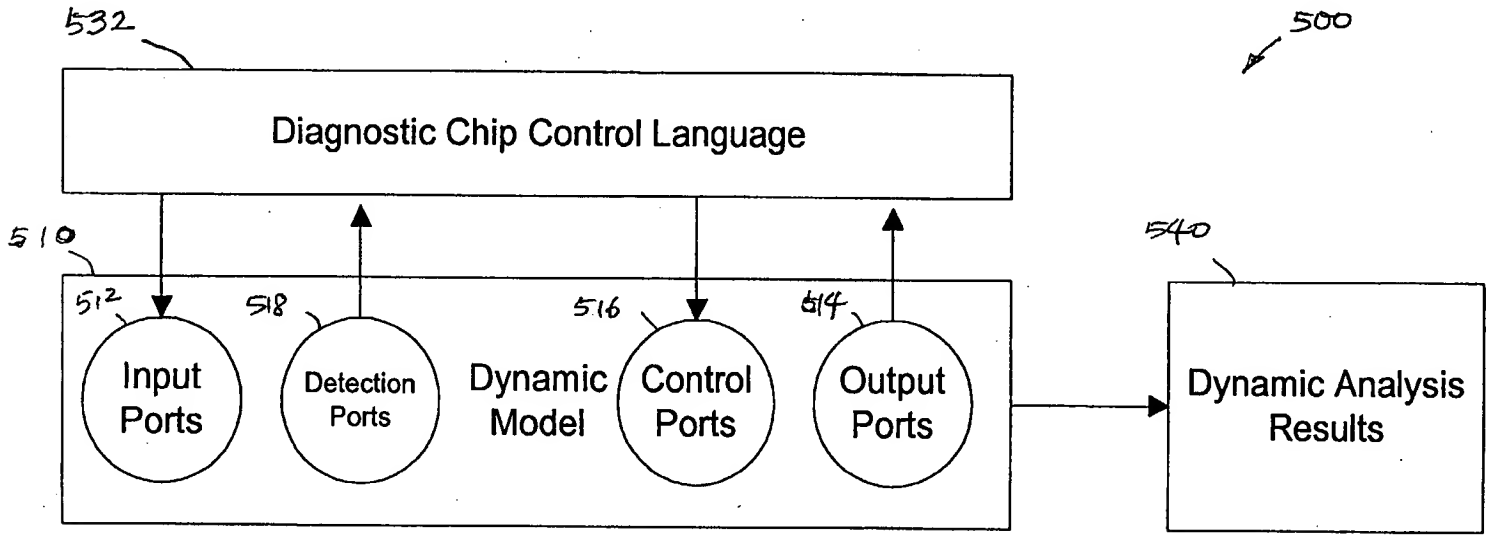

FIG. 5